

Claims

1. A recombinant *Streptomyces hygroscopicus* host cell that produces 16-desmethyl-27-desmethoxyrapamycin.
2. The compound 16-desmethyl-27-desmethoxyrapamycin in substantially pure form.
3. A recombinant *Streptomyces hygroscopicus* host cell that produces a compound selected from the group consisting of 17,18-dihydrorapamycin, 19,20-dihydrorapamycin, 21,22-dihydrorapamycin, 17,18,19,20-tetrahydrorapamycin, 17,18,21,22-tetrahydrorapamycin, 19,20,21,22-tetrahydrorapamycin, 17,18,19,20,21,22-hexahydrorapamycin, 16-demethyl-17,18-dihydrorapamycin, 16-demethyl-19,20-dihydrorapamycin, 16-demethyl-21,22-dihydrorapamycin, 16-demethyl-17,18,19,20-tetrahydrorapamycin, 16-demethyl-17,18,21,22-tetrahydrorapamycin, 16-demethyl-19,20,21,22-tetrahydrorapamycin, 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, 17-desmethyrapamycin, 23-desmethyrapamycin, 17,23-didesmethyrapamycin, 17-desmethyl-17,18-dihydrorapamycin, 17-desmethyl-19,20-dihydrorapamycin, 17-desmethyl-21,22-dihydrorapamycin, 17-desmethyl-17,18,19,20-tetrahydrorapamycin, 17-desmethyl-17,18,21,22-tetrahydrorapamycin, 17-desmethyl-19,20,21,22-tetrahydrorapamycin, 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 23-desmethyl-17,18-dihydrorapamycin, 23-desmethyl-19,20-dihydrorapamycin, 23-desmethyl-21,22-dihydrorapamycin, 23-desmethyl-17,18,19,20-tetrahydrorapamycin, 23-desmethyl-17,18,21,22-tetrahydrorapamycin, 23-desmethyl-19,20,21,22-tetrahydrorapamycin, 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 17,23-didesmethyl-17,18-dihydrorapamycin, 17,23-didesmethyl-19,20-dihydrorapamycin, 17,23-didesmethyl-21,22-dihydrorapamycin, 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, 19-methyrapamycin, 19,20-del-rapamycin, 18-hydroxyrapamycin, 18-ketorapamycin, and 18-saturated-rapamycin.

4. A compound selected from the group consisting of 17,18-dihydrorapamycin, 19,20-dihydrorapamycin, 21,22-dihydrorapamycin, 17,18,19,20-tetrahydrorapamycin, 17,18,21,22-tetrahydrorapamycin, 19,20,21,22-tetrahydrorapamycin, 17,18,19,20,21,22-hexahydrorapamycin, 16-demethyl-17,18-dihydrorapamycin, 16-demethyl-19,20-dihydrorapamycin, 16-demethyl-21,22-dihydrorapamycin, 16-demethyl-17,18,19,20-tetrahydrorapamycin, 16-demethyl-17,18,21,22-tetrahydrorapamycin, 16-demethyl-19,20,21,22-tetrahydrorapamycin, 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, 17-desmethyrapamycin, 23-desmethyrapamycin, 17,23-didesmethyrapamycin, 17-desmethyl-17,18-dihydrorapamycin, 17-desmethyl-19,20-dihydrorapamycin, 17-desmethyl-21,22-dihydrorapamycin, 17-desmethyl-17,18,19,20-tetrahydrorapamycin, 17-desmethyl-17,18,21,22-tetrahydrorapamycin, 17-desmethyl-19,20,21,22-tetrahydrorapamycin, 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 23-desmethyl-17,18-dihydrorapamycin, 23-desmethyl-19,20-dihydrorapamycin, 23-desmethyl-21,22-dihydrorapamycin, 23-desmethyl-17,18,19,20-tetrahydrorapamycin, 23-desmethyl-17,18,21,22-tetrahydrorapamycin, 23-desmethyl-19,20,21,22-tetrahydrorapamycin, 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, 17,23-didesmethyl-17,18-dihydrorapamycin, 17,23-didesmethyl-19,20-dihydrorapamycin, 17,23-didesmethyl-21,22-dihydrorapamycin, 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, 19-methylrapamycin, 19,20-del-rapamycin, 18-hydroxyrapamycin, 18-ketorapamycin, and 18-saturated-rapamycin, in substantially pure form.

5. A recombinant *Streptomyces hygroscopicus* host cell that expresses a hybrid PKS composed of at least a portion of a rapamycin PKS and at least a portion of a heterologous PKS.

6. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue.

7. A recombinant *Streptomyces hygroscopicus* host cell that expresses a PKS composed of only a portion of a rapamycin PKS.

8. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue produced by a hybrid PKS composed of at least a portion of a rapamycin PKS and at least a portion of a heterologous PKS.

9. A recombinant *Streptomyces hygroscopicus* host cell that does not express at least one rapamycin modification enzyme but does produce a rapamycin analogue produced by a PKS consisting essentially of only a portion of a rapamycin PKS.

10. The recombinant *Streptomyces hygroscopicus* host cell of claim 6 in which rapI gene, rapJ, rapM, or rapQ has been deleted or inactivated.

11. The recombinant *Streptomyces hygroscopicus* host cell of claim 10 in which rapI gene, rapJ, rapM, or rapQ has been deleted or inactivated.

12. The recombinant *Streptomyces hygroscopicus* host cell of claim 11 in which rapN and rapO have been deleted or inactivated.

13. The recombinant *Streptomyces hygroscopicus* host cell of claim 12 in which rapN, rapO and rapM have been deleted or inactivated.

14. The recombinant *Streptomyces hygroscopicus* host cell of claim 13 in which rapM, rapN, rapO, and rapQ have been deleted or inactivated.

15. The recombinant *Streptomyces hygrosopicus* host cell of claim 14 in which rapL, rapM, rapN, rapO, and rapQ have been deleted or inactivated.

16. The recombinant *Streptomyces hygrosopicus* host cell of claim 6 that produces 16-desmethyl-27-desmethoxyrapamycin.

17. The recombinant *Streptomyces hygrosopicus* host cell of claim 6 that expresses a rapamycin PKS derivative in which at least one domain of one module of the is deleted or inactivated, wherein said cells does not comprise a rapamycin PKS derivative that contains a heterologous PKS domain, module, or protein.

18. A method of making a rapamycin analog comprising culturing a host cell of claim 6 under conditions where the analog is produced.

19. The method of claim 18 wherein the rapamycin analog is 16-desmethyl-27-desmethoxyrapamycin.

20. 16-desmethyl-27-desmethoxyrapamycin produced by a method comprising culturing a host cell of claim 16 under conditions where 16-desmethyl-27-desmethoxyrapamycin is produced.